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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/880,702	06/13/2001	Katherine A. High	0800-0024	5537

31048 7590 04/28/2003

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EXAMINER
WHITEMAN, BRIAN A

ART UNIT	PAPER NUMBER
1635	10

DATE MAILED: 04/28/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/880,702	Applicant(s) HIGH, KATHERINE A.	
	Examiner Brian Whiteman	Art Unit 1635	

-- The MAILING DATE of this c mmunication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 4-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 June 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3,6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Seq. Compliance Letter* .

DETAILED ACTION

Non-Final Rejection

Claims 1, 2, 4-26 are pending.

The amendment to claims 1 and 13, the cancellation of claim 3 in paper no. 9 is acknowledged.

Noncompliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

If the applicants do not comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures in the response to this office action, the response will be considered non-responsive.

Election/Restrictions

Applicant's election with traverse of Group I and species Factor IX in Paper No. 9 is acknowledged. The traversal is on the ground(s) that the limitation of non-therapeutic polypeptide and therapeutic polypeptide is non-existent. This is found persuasive because applicant amended claim 1 and the amendment makes the restriction moot.

Since the restriction is moot, claim 2 is rejoined with the claimed invention.

Drawings

The drawings, filed on 6/13/01 have been disapproved by the draftsperson. A proper drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The correction to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 2, 4, 5, 6, 7, 8, 9, 10, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25 and 26 are rejected under 35 U.S.C. 102(a) as being anticipated by Kay et al. (IDS, Nature, 24: 257-261, March 2000) as evident by Couto et al. (US Patent 6,200,560). Kay teaches a method of gene transfer of human factor IX in haemophilia B patients with an AAV vector using intramuscularly injection (abstract). Administering the rAAV to the muscle of a human would result in the rAAV being injected into a blood vessel and slow twitch muscle fibers.

In addition, Couto teaches that 85% of the human population is seropositive for AAV-2 serotype (column 12). Thus, the method taught by Kay would anticipate delivering Factor IX to a human with AAV-2 antibodies since the vast majority of humans would be expected to be AAV-2 seropositive.

Claims 1, 2, 4, 8, 9, 10, 11, 12, 13, 14, 21, and 24 are rejected under 35 U.S.C. 102(e) as being anticipated by Couto et al. (US Patent 6,200,560). Couto teaches a method of treating hemophilia in a mammal comprising: a) providing recombinant adeno-associated virus virions (rAAV) comprising a nucleotide sequence encoding Factor VIII operably linked to expression control elements; and b. administering said rAAV to a mammal under conditions that result in the expression of Factor VIII protein at a level that provides a therapeutic effect in said mammal, wherein said rAAV is delivered to the liver (columns 51-52). Other tissues, however, may be suitable for the expression of Factor VIII even if they are not the tissue that normally synthesizes the protein. Muscle cells, for example, have been shown to express biologically active blood clotting Factor IX even though it is normally synthesized in the liver (columns 18-19). Administering the rAAV to the muscle of a human would result in the rAAV being injected into fast and slow twitch muscle fibers of the muscle. Couto teaches expressing the Factor VIII protein in human cells (abstract and columns 4-5). Couto further teaches that 85% of the human population is seropositive for AAV-2 serotype (column 12). Thus, since 85% of the human population is AAV-2 serotype positive, Couto methods would anticipate delivering a heterologous nucleotide sequence encoding a blood coagulation protein to humans having pre-existing AAV-2 antibodies.

Claims 1, 2, 4, 5, 6, 7, 8, 9, 10, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25 and 26 are rejected under 35 U.S.C. 102(e) as being anticipated by High et al. (IDS, US Patent 6,093,392 as evident by Couto et al. (US Patent 6,200,560). High teaches a method of treating hemophilia in

a human comprising: a) providing a recombinant adeno-associated virus vector (rAAV), said rAAV comprising a nucleic acid encoding human Factor IX operably linked to an expression control; and b) administering an amount of said rAAV to a mammal wherein said Factor IX is expressed at levels having a therapeutic effect on said human and wherein said therapeutic effect is an increase in coagulation of blood (column 29). High teaches administering the rAAV to the muscle tissue of the human (column 30). Administering the rAAV to the muscle of a human would result in the rAAV being injected into fast and slow twitch muscle fibers of the muscle.

Couto teaches that 85% of the human population is seropositive for AAV-2 serotype (column 12). Thus, the method taught by High would anticipate delivering Factor IX to a human with AAV-2 antibodies since the vast majority of humans would be expected to be AAV-2 seropositive.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 11, and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kay et al. (IDS, Nature, 24: 257-261, March 2000) in view further of Couto et al. (US Patent 6,200,560). Kay teaches a method of gene transfer of human factor IX in haemophilia B patients with an AAV vector using intramuscularly injection (abstract). Administering the rAAV to the muscle of a human would result in the rAAV being injected into fast and slow twitch muscle fibers of the muscle. The art of record teaches that 85% of the human population is seropositive for AAV-2 serotype. Thus, the method taught by Kay would anticipate delivering Factor IX to a human with AAV-2 antibodies since the vast majority of humans would be expected to be AAV-2 seropositive. However, Kay does not specifically teach a method of administering a rAAV to a human, wherein the delivery of said rAAV is by injecting into a duct of the liver.

However, at the time the invention was made, Couto teaches a method of treating hemophilia in a mammal comprising: a) providing recombinant adeno-associated virus virions (rAAV) comprising a nucleotide sequence encoding Factor VIII operably linked to expression control elements; and b. administering said rAAV to a mammal under conditions that result in the expression of Factor VIII protein at a level that provides a therapeutic effect in said mammal,

wherein said rAAV is delivered to the liver (columns 51-52). Other tissues, however, may be suitable for the expression of Factor VIII even if they are not the tissue that normally synthesizes the protein. Muscle cells, for example, have been shown to express biologically active blood clotting Factor IX even though it is normally synthesized in the liver (columns 18-19). Administering the rAAV to the muscle of a human would result in the rAAV being injected into fast and slow twitch muscle fibers of the muscle. Couto teaches expressing the Factor VIII protein in human cells (abstract and columns 4-5).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to administer at least one rAAV virion comprising a vector comprising a promoter operably linked to a nucleotide sequence encoding a Factor IX protein to the liver of a human. One of ordinary skill in the art would have been motivated to introduce at least one rAAV virion comprising a nucleotide sequence encoding a coagulation protein to the liver of a human with hemophilia because Couto teaches that administering a rAAV comprising a nucleotide sequence encoding a coagulation protein to the liver can treat hemophilia in the human.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (703) 305-0775. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader, SPE - Art Unit 1635, can be reached at (703) 308-0447.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Brian Whiteman
Patent Examiner, Group 1635

Scott D. Priebe

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER

Application No.: 09/880,702

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

- [X] 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.
- [X] 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).
- [X] 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).
- [ ] 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."
- [ ] 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).
- [ ] 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).
- [X] 7. Other: There are nucleotides on page 17 that do not have a SEQ ID NO:.

Applicant Must Provide:

- [X] An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".
- [X] An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.
- [X] A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
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